the heavy chain CDRs (CDR1, CDR2 and CDR3) of monoclonal antibody 7B11 (ATCC Accession No. HB-12195).

304. (New) The antibody or antigen-binding fragment of Claim 303 wherein said antibody or fragment is a humanized immunoglobulin or antigen-binding fragment thereof comprising the light chain CDRs (CDR1, CDR2 and CDR3) and the heavy chain CDRs (CDR1, CDR2 and CDR3) of monoclonal antibody 7B11 (ATCC Accession No. HB-12195) and a human framework region.

305. (New) A composition comprising the antibody or antigen-binding fragment of Claim 303 and a physiologically acceptable vehicle or carrier.

306. (New) An isolated cell that produces the antibody or antigen-binding fragment of Claim 303.

307. (New) The isolated cell of Claim 306, wherein said isolated cell is a hybridoma.

REMARKS

Claims 38, 39, 49-51, 53, 55 and 57-150 have been cancelled, and new Claims 151-307 have been added.

Support for New Claims

Claims 151-212 and 221-291

New Claims 151-212 and 221-291 are drawn to an antibody or antigen-binding fragment thereof having binding specificity for a naturally-occurring mammalian C-C chemokine receptor 3 protein, compositions comprising the antibody or antigen-binding fragment, and isolated cells that produce the antibody or antigen-binding fragment. These claims recite structural features (percent amino acid sequence identity to a reference sequence, encoded by a nucleic acid that hybridizes to a reference sequence) and functional features (has binding specificity for particular chemokines) that define the naturally-occurring mammalian C-C chemokine receptor 3 protein.

Support for the naturally-occurring mammalian C-C chemokine receptor 3 protein having at least about 90% amino acid sequence identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6 is found, for example, at page 23, line 29 through page 24, line 4; Figure 1A-1C; Figure 2A-2C; and the Sequence Listing.

Support for the naturally-occurring mammalian C-C chemokine receptor 3 protein having binding specificity for RANTES and/or MCP-3 is found, for example, at page 22, line 8; page 19, line 31 through page 20, line 2; and page 109, line 19 through page 111, line 13.

Support for the naturally-occurring mammalian C-C chemokine receptor 3 protein having binding specificity for eotaxin, MCP-2 and/or MCP-4 is found, for example, at page 22, line 8; page 20, lines 3-6; and page 99, line 21 through page 100, line 29.

Support for the antibody or antigen-binding fragment inhibiting binding of a ligand to naturally-occurring mammalian C-C chemokine receptor 3 protein is found, for example, at page 35, line 30 through page 36, line 9.

Support for the antibody or antigen-binding fragment competing with monoclonal antibody 7B11 for binding to a mammalian C-C chemokine receptor 3 protein is found, for example, at page 36, lines 10-19.

Support for the C-C chamokine receptor 3 protein being a naturally-occurring human C-C chemokine receptor 3 protein is found, for example, at page 30, line 20 *et seq.*

Support for the antibody or antigen-binding fragment being a Fab fragment, Fab' fragment, $F(ab')_2$ fragment or Fv fragment is found, for example, at page 38, line 23 through page 39, line 2.

Support for the antibody or antigen-binding fragment being a humanized antibody, a chimeric antibody, an antigen-binding fragment of a humanized antibody or an antigen-binding fragment of a chimeric antibody is found, for example, at page 37, line 19 *et seq.*

Support for the naturally-occurring mammalian C-C chemokine receptor 3 protein being encoded by a nucleic acid that hybridizes with SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or the complement of SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:5 is found, for example, at page 23, lines 10-28; Figure 1A-1C; Figure 2A-2C; and the Sequence Listing.

Support for the hybridization conditions recited in Claims 221, 234, 246, 257, 267 and 280, is found at page 104, lines 18-28.

Support for the hybridization conditions recited in Claims 230, 242, 253, 263, 276 and 288, is found at page 78, lines 11-23.

Support for the naturally-occurring mammalian C-C chemokine receptor 3 protein being encoded by SEQ ID NO: 1, 3, or 5, is found, for example, at page 23, lines 10-28.

Support for the claimed compositions (Claims 160, 172, 182, 191, 201, 210, 231, 243, 254, 264, 277 and 289) is found, for example, at page 70, lines 10-26.

Support for the claimed isolated cells and hybridomas (Claims 161, 162, 173, 174, 183, 184, 192, 193, 202, 203, 211, 212, 232, 233, 244, 245, 255, 256, 265, 266, 278, 279, 290 and 291) is found, for example, at page 36, line 33 *et seq.*

Claims 213-221

New Claims 213-221 are drawn to an antibody or antigen-binding fragment thereof having binding specificity for a naturally-occurring mammalian C-C chemokine receptor 3 protein, compositions comprising the antibody or antigen-binding fragment, and isolated cells that produce the antibody or antigen-binding fragment. These claims recite that the naturally-

occurring mammalian C-C chemokine receptor 3 protein comprises SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6. Support for these claims is found, for example, at page 23, line 29 through page 24, line 4; Figure 1A-1C; Figure 2A-2C; and the Sequence Listing.

Support for the claimed compositions (Claims 214 and 218) is found, for example, at page 70, lines 10-26.

Support for the claimed isolated cells and hybridomas (Claims 215, 216, 219 and 220) is found, for example, at page 36, line 33 *et seq.*

Claims 292-299

New Claims 292-299 are drawn to an antibody or antigen-binding fragment thereof having binding specificity for a naturally-occurring mammalian C-C chemokine receptor 3 protein, compositions comprising the antibody or antigen-binding fragment, and isolated cells that produce the antibody or antigen-binding fragment. These claims recite that the naturally-occurring mammalian C-C chemokine receptor 3 protein is encoded by SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:5. Support for these claims is found, for example, at page 23, lines 10-28; Figure 1A-1C; Figure 2A-2C; and the Sequence Listing.

Support for the claimed compositions (Claims 293 and 297) is found, for example, at page 70, lines 10-26.

Support for the claimed isolated cells and hybridomas (Claims 294, 295, 298 and 299) is found, for example, at page 36, line 33 *et seq.*

Claims 300-307

New Claims 300 and 307 are drawn to antibody 7B11 or an antigen-binding fragment thereof, an antibody or antigen-binding fragment that comprises the complementarity determining regions of antibody 7B11, compositions comprising the antibodies or antigen-binding fragments, and isolated cells that produce the antibodies or antigen-binding fragments.

Support for the claimed antibodies and cells is found, for example, at page 17, lines 19-25; page 36, line 33 *et seq.*; and page 39, line 22 through page 40, line 3.

Support for the claimed compositions (Claims 301 and 305) is found, for example, at page 70, lines 10-26.

New Claims 151-307 are supported by the application as filed. Therefore, this Amendment adds no new matter. Additional remarks are set forth below.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 38-39, 49-51, 53, 55, 57, 58, 75, 76, 81, 86, 89, 90, 91, 92-103, 143-145 and 148-150 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not disclosed in the specification in such a manner as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner states that specification discloses antibodies and antigen-binding fragments thereof that bind human C-C chemokine receptor 3 protein, and that antibodies that bind to these amino acid sequences meet the written description requirement of 35 U.S.C. § 112. (Office Action at page 3, lines 7-10.) The Examiner further states that the claims encompass antibodies and antigen-binding fragments that bind mammalian homologues of the disclosed human amino acid sequences having undisclosed amino acid sequences. (Office Action at page 3, lines 10-12.) The Examiner concludes that the application does not comply with the written description requirement because the skilled artisan cannot envision the detailed structure of the mammalian homologues, and therefore the claimed antibodies and antigen-binding fragments also cannot be envisioned and conception is not achieved until reduction to practice has occurred. (Office Action at page 4, lines 1-7.)

Claims 38-39, 49-51, 53, 55, 57, 58, 68-103, and 119-150 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not disclosed in the specification in

such a manner as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner states that the claims are genus claims which encompass antibodies and antigen-binding fragements that bind a C-C chemokine receptor 3 protein that is encoded by a nucleic acid that hybridizes to a second nucleic acid consisting of the nucleotide sequence of SEQ ID NO:1, 3 or 5. (Office Action at page 5, lines 8-11.) The Examiner states that the claims are drawn to antibodies and antigen-binding fragments directed to numerous structural variants and that the genus is highly variant. (Office Action at page 5, lines 16-19.) The Examiner concludes that one of skill in the art would conclude that the disclosure fails to provide a representative number of species to describe the genus. (Office Action at page 6, lines 6-7.)

With respect to both rejections, the Examiner directs Applicants' attention to Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement, 66 FR 1099 ("Guidelines").

Claims 38, 39, 49-51, 53, 55 and 57-150 have been cancelled, rendering the rejections moot. New Claims 151-307 are supported by adequate written description for the reasons discussed below.

The written description requirement is satisfied when the specification describes the claimed invention in sufficient detail so that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Vas-Cath, Inc. v. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). According to the Guidelines, possession of the invention can be shown by "describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention." Guidelines at 1104 (citation omitted). "The description need only describe in detail that which is new or not conventional." Guidelines at 1106 (citation omitted). "An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, *i.e.*, complete or partial structure, other physical and/or chemical properties, functional

characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. (citations omitted). The PTO has published training materials that illustrate application of the Guidelines. (Revised Interim Written Description Guidelines Training Materials, available on line at http://www.uspto.gov/web/offices/pac/writtendesc.pdf.) ("Training Materials").

The Court of Appeals for the Federal Circuit recently adopted the PTO standard, articulated in the Guidelines and illustrated in the Training Materials, for determining compliance with the written description requirement for an invention that is described functionally. Enzo Biochem, Inc. v. Gen-Probe Incorporated, 01-1230, *11-12 (Fed. Cir., July 15, 2002)(Fed. Cir. BBS) ("We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description requirement.").

The Training Materials include Example 16, which illustrates the application of the Guidelines in determining if a claim to an antibody is supported by an adequate written description.

Example 16

Example 16 on page 59 of the Training Materials relates to written description of claims drawn to an antibody that binds antigen X. The specification is said to teach antigen X as purified by gel filtration and characterize the antigen as having a molecular weight of 55 kD. (Training Materials at 59.) The specification is said to contemplate, but not teach in an example, antibodies that specifically bind to antigen X and asserts that such antibodies can be used in assays to detect HIV. (Training Materials at 59.) The Example states that the "general knowledge in the art is such that antibodies are structurally well characterized," and that it is "well known that antibodies can be made against virtually any protein." (Training Materials at 59.) The application is said to contain the following claim:

An isolated antibody capable of binding to antigen X.

(Training Materials at 59.)

The claim is drawn to a genus encompassing any antibody that binds antigen X. The analysis presented in Example 16 states that antigen X is novel and unobvious. (Training Materials at 60.)

Regarding written description of the claimed subject matter, the Example states:

> Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.

(Training Materials at page 60.) Thus, the disclosure in this Example provides an adequate written description of the claimed antibodies. (Training Materials at page 60.)

Based upon the analysis and conclusion of Example 16 of the Training Materials, the question of whether the subject claims are supported by an adequate written description focuses on whether the naturally-occurring mammalian (or human) C-C chemokine receptor 3 protein, as defined in the claims, is described with sufficient detail so that one skilled in the art would reasonably conclude that Applicants were in possession of the protein at the time the application was filed.

In the new claims, the naturally-occurring mammalian or naturally-occurring human C-C chemokine receptor 3 protein is defined as having structural features or physical/chemical properties (e.g., amino acid sequence identity with a reference sequence, encoded by a nucleic acid that hybridizes to a reference nucleic acid) and functional features (binding specificity for a particular chemokine). Therefore, a determination of whether the specification contains an adequate written description must focus on whether the specification conveys to those skilled in the art that Applicants were in possession of naturally-occurring mammalian or naturally-occurring human C-C chemokine receptor 3 proteins having the properties recited in the claims when the application was filed. Examples 9 and 14 of the Training Materials are instructive in this regard.

Claims That Recite % Amino Acid Sequence Identity

Example 14 on page 53 of the Training Materials relates to written description of claims drawn to a protein and variants thereof which have a specified catalytic activity. In particular, in Example 14, the specification is said to disclose a single protein determined to have the amino acid sequence of SEQ ID NO:3, that catalyzes the reaction A → B, and contemplates, but does not exemplify, variants having all or any of the following: substitutions, insertions and deletions. (Training Materials at page 53.) The specification is further said to indicate that procedures for producing such variants are conventional in the art and to disclose an assay for detecting the catalytic activity of the protein. (Training Materials at page 53.) The application is said to contain the following claim:

> A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B.

(Training Materials at page 53.)

The claim is drawn to a genus of proteins that are defined by function (catalyze the reaction of A → B) and structural features (SEQ ID NO:3, at least 95% identical to SEQ ID NO:3). The analysis presented in Example 14 states that the claim has two generic embodiments: (1) a protein which comprises SEQ ID NO:3; and (2) variants of SEQ ID NO:3. (Training Materials at page 54.)

The analysis present in Example 14, focuses on whether the specification satisfies the written description requirement by describing a representative number of species within the genus. "Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." Guidelines, 66 FR at 1106.

According to the analysis, SEQ ID NO:3 is novel and nonobvious, and was actually reduced to practice. (Training Materials at page 54.) In addition, the specification and claim are said to reveal that:

1) the genus of proteins that are variants of SEQ ID NO:3 does not have substantial variation because all variants must have at least 95% identity to SEQ ID NO:3 and must have the specified activity; and

2) the single disclosed species (SEQ ID NO:3) is representative of the claimed genus because all members of the genus have at least 95% identity to SEQ ID NO:3 and because an assay suitable for identifying all variants that have the specified activity is disclosed. (Training Materials at page 54.)

Based on these findings, the specification in Example 14 of the Training Materials is said to meet the written description requirement of 35 U.S.C. § 112 for the claim. (Training Materials at page 55.)

The claims of the subject application that recite % amino acid sequence identity are similar to Example 14 of the Training Materials in that the claims define the naturally-occurring mammalian (or human) C-C chemokine receptor 3 proteins by function (e.g., binds RANTES, MCP-3, eotaxin, MCP-2, MCP-4) and structural features (e.g., at least about 90% amino acid sequence identity to SEQ ID NO:2, 4 or 6). However, the subject application contains a more extensive written description of the claimed invention than does the specification in Example 14 of the Training Materials. For example, the application discloses three species of mammalian C-C chemokine receptor 3 proteins by amino acid sequence (SEQ ID NO:2, 4 and 6) (see, e.g., Figure 1A-1C, Figure 2A-2C, and Sequence Listing), multiple methods for assessing binding to naturally-occurring mammalian C-C chemokine receptor 3 protein (See, e.g., page 109, line 19 through page 111, line 13), and describes the broader class of naturally-occurring mammalian C-C chemokine receptor 3 protein by describing a combination of functional and structural or physical/chemical features which are sufficient to distinguish the members of the genus from other materials.

Applying the analysis from Example 14 of the Training Materials to the claims of the subject application that recite percent amino acid sequence identity reveals:

1) the genus of naturally-occurring mammalian (or human) C-C chemokine receptor 3 proteins does not have substantial variation because all proteins must have the

specified binding activity and have at least 90% amino acid sequence identity with SEQ ID NO: 2, 4 or 6; and

2) the three disclosed species (SEQ ID NO: 2, 4 and 6) are representative of the genus because all members of the genus have at least 90% amino acid sequence identity with SEQ ID NO:2, 4 or 6, the specified binding activity was exemplified in the application for SEQ ID NO:2 and 4, and assays suitable for identifying proteins that have the specified binding activity are disclosed.

Therefore, like in Example 14 of the Training Materials, the instant specification provides adequate written description for claims that recite percent amino acid sequence identity.

Claims that Recite Hybridization Conditions

Example 9 on page 35 of the Training Materials relates to written description of claims drawn to nucleic acids that are defined as hybridizing to a reference nucleic acid, and encoding a protein which binds a receptor and stimulates its activity. In particular, in Example 9 of the Training Materials, the specification is said to disclose a single cDNA (SEQ ID NO:1) which encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity. (Training Materials at page 35.) The specification is further said to include an example where the complement of SEQ ID NO:1 was used under specified hybridization conditions to isolate additional nucleic acids that have the biological activity of SEQ ID NO:1. (Training Materials at page 35.) The hybridizing nucleic acids were not sequenced, but they were expressed and several were shown to encode proteins that bind to the receptor and stimulate adenylate cyclase activity. The Example further states that the hybridizing nucleic acids that encode proteins that bind to the receptor and stimulate adenylate cyclase activity may or may not be the same as SEQ ID NO:1. (Training Materials at page 35.) The application is said to contain the following claim:

> An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO:1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

(Training Materials at page 35-36.)

The claim is drawn to a genus of nucleic acids that are defined by function (encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity) and physical/chemical properties (hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO:1).

The analysis present in Example 9 of the Training Materials, focuses on whether the specification satisfies the written description requirement by describing a representative number of species within the genus. "Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." Guidelines, 66 FR at 1106.

According to the analysis, SEQ ID NO:1, the single disclosed species encompassed by the claimed genus, is novel and nonobvious and was actually reduced to practice. (Training Materials at page 36.) In addition, the specification and claim are said to reveal that:

1) the person of skill in the art would not expect substantial variation among species encompassed by the claimed genus because the highly stringent conditions recited in the claim yield structurally similar DNAs; and

2) highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill in the art are adequate to allow the person skilled in the art to determine that Applicant was in possession of the claimed invention.

(Training Materials at page 36-37.)

Based on these findings, the specification in this Example is said to disclose a representative number of species, and the written description requirement of 35 U.S.C. § 112 is satisfied. (Training Materials at page 37.)

Applying the analysis from Example 9 of the Training Materials to the claims of the subject application that recite hybridization conditions reveals that three species encompassed by the claims are disclosed (SEQ ID NO:1, 3 and 5):

1) the person of skill in the art would not expect substantial variation among species encompassed by the claimed genus because the moderate and high stringency

hybridization conditions recited in the claim yield structurally similar DNAs that encode naturally-occurring mammalian (or human) C-C chemokine receptor 3 proteins having the specified binding activity; and

2) the hybridization conditions in combination with the coding function of DNA and the level of skill in the art are adequate to allow the person skilled in the art to determine that Applicants were in possession of the claimed invention.

Therefore, like in Example 9 of the Training Materials, the instant specification provides adequate written description for claims that recite hybridization conditions.

Claim Rejections Under 35 U.S.C. 112, Second Paragraph

Claims 38, 39, 49-51, 53, 55, 57, 58, 68-103 and 119-150 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner states that the claims are indefinite in the recitation of "moderate stringency" or "high stringency" conditions.

Claims 38, 39, 49-51, 53, 55, 57, 58, 68-103 and 119-150 have been cancelled, rendering the rejection moot. The new claims recite hybridization conditions as suggested by the Examiner.

Claim Rejections Under 35 U.S.C. § 103

Claims 38, 39, 49, 50, 70, 71, 73 and 75 are rejected under 35 U.S.C. § 103 as being obvious over Yamagami *et al.* (*Biochem. Biophys. Res. Commun. 202*(2):1156-1162 (1994)) in view of Lerner (*Nature 299*:592-596 (1982)) and Harlow *et al.* (Antibodies: A Laboratory Manual, Chapter 5, page 76, Cold Spring Harbor Laboratory (1988)). The Examiner states that Yamagami *et al.* disclose the cDNA cloning of a human monocyte chemoattractant protein 1 receptor which has a stretch of 10 amino acids which are identical with a portion of the amino acid sequence depicted in SEQ ID NO: 2 of the present application and that the stretch of identical amino acids is not part of the transmembrane domain. The Examiner further states that Lerner teaches the production of antibodies from known polypeptides, wherein the antibody can have predetermined specificity and that antibodies made against a predetermined peptide are

useful in studying the protein conformation of the intact protein from which the immunizing peptide was cleaved. The Examiner also states that Harlow *et al.* teach that peptides of six residues in length will consistently elicit antibodies that bind to the original protein. The Examiner concludes that it would have been *prima facie* obvious to one having ordinary skill in the art to use the amino acid sequence taught by Yamagami *et al.* to produce monoclonal and polyclonal antibodies with a predetermined specificity as taught by Lerner with the expectation that the antibodies made against proteins with sequence identity to SEQ ID NO: 2 would be useful in understanding the conformational changes the receptor undergoes during activation by a natural ligand.

Claims 38, 39, 49, 50, 70, 71, 73 and 75 have been cancelled, rendering the rejections moot. New Claims 151-307 are not obvious over the combined teachings of the cited references for the reasons discussed below.

For clarity, the teaching of the cited references are summarized below.

Yamagami et al.

Yamagami *et al.* disclose the cloning and amino acid sequence of a human monocyte chemoattractant protein 1 receptor (MCP-1RB, CCR2B). Yamagami *et al.* does not disclose an antibody or antigen-binding fragment that binds MCP-1RB.

The Examiner states that the sequence of Yamagami *et al.* contains regions that have amino acid sequence identity with portions of SEQ ID NO:2. However, neither Yamagami *et al.* nor any other prior art reference of record discloses the amino acid sequence of a naturally-occurring mammalian CCR3 (e.g., SEQ ID NO:2). Thus, the Examiner's observation is made with the benefit of Applicants' disclosure and is, therefore, based on impermissible hindsight.

Lerner

Lerner teaches the production of antibodies raised against a peptide that bind a known polypeptide from which the peptide is derived, and that such antibodies are useful in studying the protein conformation of the intact protein from which the immunizing peptide was cleaved.

Harlow et al.

Harlow *et al.* teach that "[t]he smallest synthetic peptides that will consistently elicit antibodies that bind the original protein are 6 residues in length." (Harlow *et al.* at page 76, first sentence under the heading "Size of the Peptide.")

None of the references cited by the Examiner disclose an antibody or antigen-binding fragment that binds naturally-occurring mammalian C-C chemokine receptor 3 protein (or even human monocyte chemoattractant protein 1 receptor). Therefore, the rejection proposes that it would have been obvious at the time the claimed invention was made to produce an anti-peptide antibody that binds the human monocyte chemoattractant protein 1 receptor of Yamagami *et al.* using a peptide derived from that receptor, and that such an antibody would inherently bind naturally-occurring mammalian C-C chemokine receptor 3 protein (e.g., SEQ ID NO:2).

The rejection is legally improper. When a claimed invention is rejected as obvious in view of a combination of references, §103 requires that (1) "the prior art would have suggested to those of ordinary skill in the art that they should ... carry out the claimed process"; and (2) the prior art should establish a reasonable expectation of success. In re Vaeck, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." Id. (Emphasis added). Obviousness cannot be predicated on what was unknown at the time the invention was made. In re Rijckaert, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).

Here, the prior art cited by the Examiner discloses the amino acid sequence of a human monocyte chemoattractant protein 1 receptor and provides general teachings regarding anti-peptide antibodies and uses for such antibodies. However, the cited prior art does not teach the amino acid sequence of a naturally-occurring mammalian C-C chemokine receptor 3 protein (e.g., SEQ ID NO:2) or that the sequence of Yamagami *et al.* contains regions that have amino acid sequence identity with portions of SEQ ID NO:2. Further, there is nothing in the combined teaches of the cited references that would have lead the person of ordinary skill in the art at the time the invention was made to select particular peptides, which have amino acid sequence

identity with the as yet undiscovered SEQ ID NO:2, from the amino acid sequence of the receptor of Yamagami *et al.* for use in preparing anti-peptide antibodies. In view of these deficiencies in the teachings of the prior art, the cited references do not provide the requisite reasonable expectation of success in producing an antibody or antigen-binding fragment that has binding specificity for a naturally-occurring mammalian C-C chemokine receptor 3 protein by following the combined teachings of Yamagami *et al.*, Lerner and Harlow *et al.*

In regard to the Examiner's proposition that an anti-peptide antibody that binds the human monocyte chemoattractant protein 1 receptor of Yamagami *et al.* would inherently bind a naturally-occurring mammalian C-C chemokine 3 protein, it is pointed out that "[i]nherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient [to establish inherency]." In re Robertson, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999) (citation omitted).

Thus, even if it were possible to prepare an anti-peptide antibody that binds a naturally-occurring mammalian C-C chemokine receptor 3 protein using particular peptides from the human monocyte chemoattractant protein 1 receptor of Yamagami *et al.* at the time the invention was made, inherency would not be established, because the possibility that a result may be realized from a given set of circumstances is not sufficient to establish inherency.

Again, it is noted that the amino acid sequence of naturally-occurring mammalian C-C chemokine receptor 3 protein is not found in the prior art, and that the prior art does not teach that the amino acid sequence of the human monocyte chemoattractant protein 1 receptor of Yamagami *et al.* contains regions that have amino acid sequence identity with portions of SEQ ID NO:2. Thus, the rejection relies on impermissible hindsight provided by Applicants' disclosure.

Reconsideration and withdrawal of the rejection for the reasons stated above and those stated in the Second Preliminary Amendment filed on September 26, 2000 are requested.

Supplemental Information Disclosure Statement

A Supplemental Information Disclosure Statement (SIDS) is being filed concurrently herewith. Acknowledgment of consideration of the information provided therein is requested in the next Office Communication.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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